HFA-305 (Docket Management Br.)

Date of Approval Letter: FEB 1 1999

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-061

DECTOMAX® (doramectin)
1% Injectable Solution for Cattle and Swine

"...effectively controls infections and protects cattle from reinfection with *Haemonchus placei* for 14 days after treatment."

Sponsored by:

Pfizer, Inc.

I. GENERAL INFORMATION

NADA Number:	141-061
Sponsor:	Pfizer, Inc. 235 East 42nd Street New York, New York 10017
Established Name:	doramectin
Trade Name:	DECTOMAX® 1% Injectable Solution for Cattle and Swine
Marketing Status:	over-the-counter (OTC)
Effect of Supplement:	New indication for persistent control of nematodes in cattle adding protection against *Haemonchus placei* for 14 days after treatment.

II. INDICATIONS FOR USE: For the treatment and control of the following in cattle.

Gastrointestinal roundworms	*Ostertagia ostertagi*	Adults and fourth-stage larvae
	Ostertagia ostertagi	Inhibited fourth-stage larvae
	Ostertagia lyrata	Adults and fourth-stage larvae
	Haemonchus placei	Adults and fourth-stage larvae
	Trichostrongylus axei	Adults and fourth-stage larvae
	Trichostrongylus colubriformis	Adults and fourth-stage larvae
	Trichostrongylus longispicularis	Adults
	Cooperia oncophora	Adults and fourth-stage larvae
	Cooperia punctata	Adults and fourth-stage larvae
	Cooperia pectinata	Adults
	Cooperia surnabada (syn. mcmasteri)	Adults and fourth-stage larvae
	Bunostomum phlebotomum	Adults
	Strongyloides papillosus	Adults
	Oesophagostomum radiatum	Adults and fourth-stage larvae
	Trichuris spp.	Adults
Lungworms	*Dictyocaulus viviparus*	Adults and fourth-stage larvae
Eyeworms	*Thelazia* spp.	Adults
Grubs	*Hypoderma bovis* *Hypoderma lineatum*	
Lice	*Haematopinus eurysternus* *Linognathus vituli* *Solenopotes capillatus*	
Mange mites	*Psoroptes bovis* *Sarcoptes scabiei*	

Dectomax injectable solution has been proved to effectively control infections and to protect cattle from reinfection with *Cooperia oncophora* and *Haemonchus placei* for 14 days; *Ostertagia ostertagi* for 21 days; and *Cooperia punctata, Oesophagostomum radiatum,* and *Dictyocaulus viviparus* for 28 days after treatment.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND DOSAGE

A. Dosage Form: DECTOMAX® 1% Injectable Solution for Cattle and Swine is a sterile solution containing 10 mg doramectin/mL.

B. Route of Administration: DECTOMAX® 1% Injectable Solution for Cattle and Swine may be administered by subcutaneous or intramuscular injection.

C. Approved Dose: 200 mcg doramectin/kg body weight (1 mL/110 lb body weigh)

IV. EFFECTIVENESS

Data demonstrating the effectiveness of DECTOMAX® 1% Injectable Solution for Cattle and Swine of previously approved indications are discussed in the parent NADA 141-061 FOI Summaries (original approval dated July 30, 1996, supplemental approvals dated July 18, 1997, September 18, 1997, and October 25, 1998). Data from the following dose confirmation trials demonstrate that DECTOMAX® 1% Injectable Solution administered at the recommended dosage protects cattle against infection or reinfection with *Haemonchus placei* for 14 days after treatment.

Note: Nematode percentage efficacies were calculated using the following formula:

[Arithmetic mean number of nematodes in control cattle) - (Arithmetic mean number of nematodes in doramectin-treated cattle)] ÷ (Arithmetic mean number of nematodes in control cattle) × 100 = Percent Effectiveness

A. Dose Confirmation: Study No. 1231C-60-95-198

1. Investigator: Dr. T.A. Yazwinski, University of Arkansas, Fayettville, Arkansas

2. General design:

   a. Purpose: To evaluate the persistent efficacy of doramectin against artificially induced infections of *Haemonchus placei.*

   b. Animals: Forty-two (42) Holstein calves (10 per group, with 2 larval viability monitors). Animals were approximately 2-6 months old and weighed 81 to 211 kg at the start of the study. All animals were treated with fenbendazole during the acclimation period to eliminate any existing infections as confirmed by negative fecal egg counts done on Day -1.

   c. Controls: Control animals received saline.

   d. Infection: Infective larvae were given to each animal daily, starting on Day 14 after treatment through Day 28. Three hundred *Haemonchus placei* larvae were administered daily. The larval viability monitors were given 10,000 *Haemonchus placei* larvae on Day 28.

d. Test article administration: The approved formulation of injectable solution containing 10 mg doramectin per mL was administered by subcutaneous injection. 1 mL/110 lb body weight (200 mcg doramectin/kg body weight) was given once to each animal in three groups. Groups T1 and T2 were treated with saline and doramectin, respectively, on Day 0. Group T3 was treated with doramectin on Day 7, and Group T4 was treated with doramectin on Day 14.

e. Pertinent variables measured: Worm counts were determined at necropsy which was 42 to 43 days after Groups T1 and T2 received treatment, 14 to 15 days after the last *Haemonchus placei* larvae were administered to all groups.

3. Results – *Haemonchus placei* was present in adequate numbers for a determination of efficacy.

Table 4.1. Arithmetic mean worm counts of *Haemonchus placei* recovered for each group, number of infected animals, and percent efficacy

				H. placei		
Group	Treatment	Day of Treatment	Persistence Interval	worm count	infected animals	percent efficacy
T1	saline	0	-	2300	10	-
T2	doramectin	0	28	610	8	73.5%
T3	doramectin	7	21	483	1	79.0%
T4	doramectin	14	14	180	0	92.2%

4. Adverse reactions: No adverse reactions to treatment were observed.

5. Conclusion: This study is adequate to establish a level of persistent efficacy for *Haemonchus placei* for 14 days.

B. Dose Confirmation: Study No. 2239A-60-97-135

1. Investigator: Lora Ballweber, D.V.M., M.S., Mississippi State, Missouri

2. General design:

a. Purpose: To evaluate the persistent efficacy of doramectin against artificially induced infections of *Haemonchus placei.*

b. Animals: Forty-two (42) crossbred beef calves (10 per group, with 2 larval viability monitors). Animals were approximately 2 to 6 months old and weighed 117 to 165 kg at the start of the study. All animals were treated with fenbendazole during the acclimation period to eliminate any existing infections as confirmed by negative fecal egg counts done on Day -1.

c. Infection: Infective larvae were given to each animal daily, starting on Day 14 after treatment through Day 28. Three hundred *Haemonchus placei* larvae were administered daily. The larval viability monitors were given 10,000 *Haemonchus placei* larvae on Day 28.

d. Test article administration: The approved formulation of injectable solution containing 10 mg doramectin per mL was administered by subcutaneous injection. 1 mL/110 lb body weight (200 mcg doramectin/kg body weight) was given once to each animal in three groups. Groups T1 and T2 were treated with saline and doramectin, respectively, on Day 0. Group T3 was treated with doramectin on Day 7 and Group T4 was treated with doramectin on Day 14.

e. Pertinent variables measured: Worm counts were determined at necropsy which was 43 to 44 days after Groups T1 and T2 received treatment, 15 to 16 days after the last *Haemonchus placei* larvae were administered to all groups.

3. Results:

Table 4.2. Mean worm counts of *Haemonchus placei* recovered for each group, number of infected animals, and percent efficacy

Group	Treatment	Day of Treatment	Persistence Interval	Worm Count	Infected Animals	Percent Efficacy
T1	saline	0	0	715	10	-
T2	doramectin	0	28	40	6	94.4%
T3	doramectin	7	21	25	1	96.5%
T4	doramectin	14	14	15	1	97.9%

4. Adverse reactions: No adverse reactions were observed during these studies.

5. Conclusion: This study is adequate to establish a level of persistent efficacy for *Haemonchus placei* for 28 days.

V. ANIMAL SAFETY

As discussed in the parent NADA 141-061 FOI Summary (approval date July 30, 1996).

VI. HUMAN SAFETY

As discussed in the parent NADA 141-061 FOI Summaries (original approval date July 30, 1996, and supplemental approval date October 25, 1998).

VII. AGENCY CONCLUSION

The data submitted in support of this supplemental NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and implementing regulations at Part 514 of Title 21, Code of Federal Regulations (21 CFR 514) to demonstrate that DECTOMAX® 1% Injectable Solution for Cattle and Swine, when used under the proposed conditions of use, is safe and effective to control infections and to protect cattle from reinfection with *Haemonchus placei* for 14 after treatment.

For cattle, tolerances of 0.1 ppm for parent doramectin (marker residue) in liver (target tissue) and 0.3 ppm in muscle are codified at 21 CFR 556.225. The preslaughter withdrawal time is 35 days following one subcutaneous or intramuscular injection of DECTOMAX® 1% Injectable Solution, as specified at 21 CFR 522.770.

The agency has concluded that this product shall retain over-the-counter marketing status because adequate directions for use have been written for the layman and the conditions for use prescribed on the label are likely to be followed in practice.

In accordance with 21 CFR 514.106(b)(2), this is a Category II change which did not require a reevaluation of the safety or effectiveness data in the parent application.

The agency has determined under 21 CFR 25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant impact on human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Under section 512(c)(2)(F)(iii) of the FFDCA, this approval for food producing animals qualifies for THREE (3) years of marketing exclusivity beginning on the date of approval because the supplemental application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence or residue studies) required for the approval of the application and conducted or sponsored by the applicant. The THREE years of marketing exclusivity applies only to the new claim for which the supplemental application is approved.

DECTOMAX® 1% Injectable Solution for Cattle and Swine is under U.S. patent number 5,089,480, which expires on February 18, 2009.

VIII. APPROVED PRODUCT LABELING (attached)

A. Facsimile label - 500-mL rubber-stoppered, glass vials

B. Facsimile package insert

000008

79-5199-00-X7 Facsimile Draft #2 11/3/98

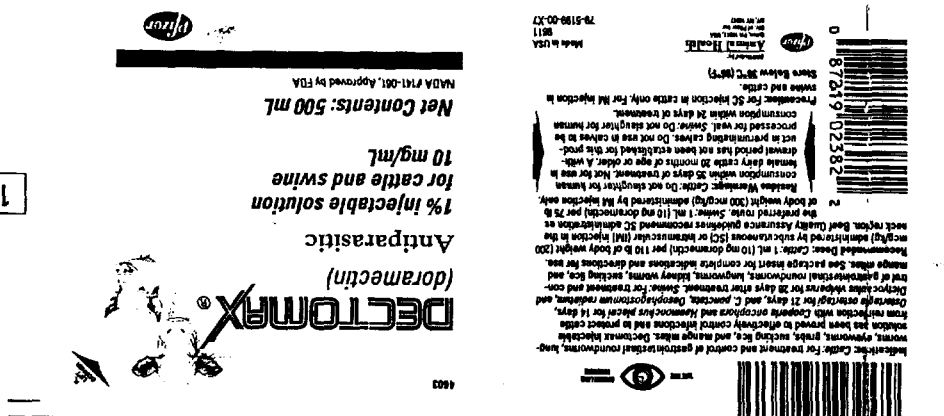
PMS 116 | PMS Reflex Blue | Black | Icon Black (60% Black)

Code 128:

7951990053

Outer Label: 7 13/16" (W) X 3 1/4" (H)

Folded Leaflet/Insert: 6 15/16" (W) X 3 1/4" (H)



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Gastrointestinal Roundworms (adults and fourth stage larvae)
Ostertagia ostertagi (including inhibited larvae)
O. lyrata
Haemonchus placei
Trichostrongylus axei
T. colubriformis
T. longispicularis[1]
Cooperia oncophora
C. pectinata[1]
C. punctata
C. surnabada (syn. *mcmasteri*)
Bunostomum phlebotomum[1]
Strongyloides papillosus[1]
Oesophagostomum radiatum
Trichuris spp.[1]
Lungworms (adults and fourth stage larvae)
Dictyocaulus viviparus
Eyeworms (adults)
Thelazia spp.
Grubs (parasitic stages)
Hypoderma bovis
H. lineatum
Sucking Lice
Haematopinus eurysternus
Linognathus vituli
Solenopotes capillatus
Mange Mites
Psoroptes bovis
Sarcoptes scabiei

[1] adults

Dectomax injectable solution has been proved to effectively control infections and to protect cattle from reinfection with *Cooperia oncophora* and *Haemonchus placei* for 14 days, *Ostertagia ostertagi* for 21 days, and *C. punctata*, *Oesophagostomum radiatum*, and *Dictyocaulus viviparus* for 28 days after treatment.

Swine: Dectomax injectable solution is indicated for the treatment and control of the following species of gastrointestinal roundworms, lungworms, kidney worms, sucking lice (see PRECAUTIONS), and mange mites. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

Gastrointestinal Roundworms (adults and fourth stage larvae)
Ascaris suum
Oesophagostomum dentatum
Oesophagostomum quadrispinulatum[1]
Strongyloides ransomi[1]
Hyostrongylus rubidus[1]
Lungworms (adults)
Metastrongylus spp.
Kidney Worms (adults)
Stephanurus dentatus
Mange Mites (adults and immature stages)
Sarcoptes scabiei var. suis
Sucking Lice (adults and immature stages)
Haematopinus suis

[1] adults

DECTOMAX®

(doramectin)

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Antiparasitic

1% injectable solution for cattle and swine
10 mg/mL

PRODUCT DESCRIPTION: Dectomax injectable solution is a ready-to-use, colorless to pale yellow, sterile solution containing 1% w/v doramectin (10 mg/mL). In cattle, Dectomax is formulated to deliver the recommended dosage (200 mcg/kg of body

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weight) when given by subcutaneous (SC) or intramuscular (IM) injection at the rate of 1 mL/110 lb of body weight. In swine, Dectomax is formulated to deliver the recommended dosage (300 mcg/kg of body weight) when given by IM injection at the rate of 1 mL/75 lb of body weight.

PRODUCT CHARACTERISTICS: Dectomax injectable solution is a highly active, broad-spectrum parasiticide for parenteral administration to cattle and swine. It contains doramectin, a novel fermentation-derived macrocyclic lactone discovered by Pfizer Inc. Doramectin is isolated from fermentations of selected strains derived from the soil organism *Streptomyces avermitilis*. A primary mode of action of macrocyclic lactones is to modulate chloride ion channel activity in the nervous system of nematodes and arthropods. Macrocyclic lactones bind to receptors that increase membrane permeability to chloride ions. This inhibits the electrical activity of nerve cells in nematodes and muscle cells in arthropods and causes paralysis and death of the parasites. In mammals, the neuronal receptors to which macrocyclic lactones bind are localized within the central nervous system (CNS), a site reached by only negligible concentrations of doramectin.

One dose of Dectomax injectable solution effectively treats and controls a wide range of roundworm and arthropod parasites that impair the health and productivity of cattle and swine.

Studies have demonstrated the safety margin of Dectomax injection in cattle and swine. In USA trials, no toxic signs were seen in cattle given up to 25 times the recommended dose, or in swine given up to 10 times the recommended dose. Studies also demonstrated safety in neonatal calves and piglets treated with up to 3 times the recommended dose. In males (bulls and boars) and females (cows and sows during folliculogenesis, implantation, organogenesis, and through gestation), a dose times the recommended dose had no effect on breeding performance.

PRODUCT INDICATIONS: *Cattle:* Dectomax injectable solution is indicated for the treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, eyeworms, grubs (see PRECAUTIONS), sucking lice (see PRECAUTIONS), and mange mites. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

DOSAGE: *Cattle:* Administer Dectomax injectable solution at the recommended dosage of 200 mcg doramectin per kg (91 mcg/lb) of body weight. Each mL contains 10 mg of doramectin, sufficient to treat 110 lb (50 kg) of body weight.

Body Weight (lb)	Dose (mL)	Body Weight (lb)	Dose (mL)
110	1	660	6
220	2	770	7
330	3	880	8
440	4	990	9
550	5	1,100	10

Swine: Administer Dectomax injectable solution at the recommended dosage of 300 mcg doramectin per kg (136 mcg/lb) of body weight. Each mL contains 10 mg of doramectin, sufficient to treat 75 lb (34 kg) of body weight.

Body Weight (lb)	Dose (mL)	Body Weight (lb)	Dose (mL)
15	0.2	150	2.0
30	0.4	225	3.0
45	0.6	300	4.0
60	0.8	375	5.0
75	1.0	450	6.0

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Cattle treated with Dectomax after the end of the heel fly season may be re-treated with Dectomax during the winter for internal parasites, mange mites, or sucking lice, without danger of grub-related reactions. A planned parasite control program is recommended.

CAUTION: Dectomax has been developed specifically for use in cattle and swine only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

ENVIRONMENTAL SAFETY: Studies indicate that when doramectin comes in contact with the soil, it readily and tightly binds to the soil and becomes inactive over time. Free doramectin may adversely affect fish and certain waterborne organisms on which they feed. Do not permit water runoff from feedlots to enter lakes, streams, or groundwater. Do not contaminate water by direct application or by the improper disposal of drug containers. Dispose of containers in an approved landfill.

Store Below 30°C (86°F)

HOW SUPPLIED: Dectomax is available in 100-mL, 250-mL, and 500-mL multi-dose, rubber-capped glass vials.

U.S. Patent No. 5,089,480

NADA #141-061, Approved by FDA

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Distributed by:

Pfizer Animal Health
Exton, PA 19341, USA
Div. of Pfizer Inc
NY, NY 10017

TAKE TIME DISCERNE LABEL DIRECTIONS

79-5199-00-X
November 199
Printed in US.

RECOMMENDED TREATMENT PROGRAM FOR SWINE: To effectively initiate control of mange and sucking lice in swine, it is important to treat all animals in the herd. After initial treatment, use Dectomax regularly as follows:

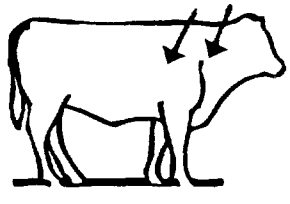
Breeding Animals:
Sows: Treat 7–14 days prior to farrowing to minimize exposure of piglets to mites and sucking lice.
Gilts: Treat 7–14 days prior to breeding. Treat 7–14 days prior to farrowing.
Boars: Treat a minimum of 2 times per year.

Feeder Pigs: Treat any new feeder pigs upon arrival at farm or before placement in clean quarters.

Weaners, Growers, Finishers: Weaners and grow-out/finisher pigs should be treated before placement in clean quarters.

For effective mange elimination, care must be taken to prevent reinfestation from exposure to untreated animals or contaminated facilities.

ADMINISTRATION: Dry, sterile equipment and aseptic procedures should be used when withdrawing and administering Dectomax. For multiple treatments either automatic injection equipment or an aspirating needle should be used.



Cattle: Administer Dectomax injectable solution by the SC or IM route. Injections should be made using a 16 gauge needle for adult cattle or an 18 gauge needle for young animals. Needles 1/2–3/4" in length are suggested for SC administration. A 1-1/2" needle is suggested for IM administration. SC injections should be administered under the loose skin in front of or behind the shoulder. IM injections should be administered into the muscular region of the neck. Beef Quality Assurance guidelines recommend SC administration as the preferred route.

Swine: Administer Dectomax injectable solution by the IM route. Inject in the neck region using an 18 gauge x 1" needle for young animals; a 16 gauge x 1-1/2" needle for sows and boars. To accurately meter doses administered to piglets, use of a tuberculin syringe and 20 gauge x 1" needle is recommended.

WARNINGS: Not for human use. Keep out of reach of children. The material safety data sheet (MSDS) contains more detailed occupational safety information. To report adverse effects in users, to obtain more information, or to obtain an MSDS, call 1-800-366-5288.

RESIDUE WARNINGS: *Cattle:* Do not slaughter for human consumption within 35 days of treatment. Not for use in female dairy cattle 20 months of age or older. A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal. *Swine:* Do not slaughter for human consumption within 24 days of treatment.

PRECAUTIONS: For SC injection in cattle only. For IM injection in swine and cattle. This product is approved for the treatment and control of sucking lice. For treatment of biting lice in cattle, use of Dectomax Pour-On is recommended.

Dectomax is highly effective against all stages of cattle grubs. However, proper timing of treatment is important. For most effective results, cattle should be treated as soon as possible after the end of the heel fly (warble) season.

Destruction of *Hypoderma* larvae (cattle grubs) at the period when these grubs are in vital areas may cause undesirable host-parasite reactions including the possibility of fatalities. Killing *H. lineatum* when it is in the tissue surrounding the gullet may cause bloat; killing *H. bovis* when it is in the vertebral canal may cause staggering or paralysis. These reactions are not specific to treatment with Dectomax, but can occur with any successful treatment of grubs. Cattle should be treated either before or after these stages of grub development. Consult your veterinarian concerning the proper time for treatment.

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DECTOMAX®

(doramectin)

Antiparasitic

1% injectable solution for cattle and swine 10 mg/mL

Net Contents: 500 mL

NADA #141-061, Approved by FDA

[redacted]

Indications: *Cattle:* For treatment and control of gastrointestinal roundworms, lungworms, eyeworms, grubs, sucking lice, and mange mites. Dectomax injectable solution has been proved to effectively control infections and to protect cattle from reinfection with *Cooperia oncophora* and *Haemonchus placei* for 14 days, *Ostertagia ostertagi* for 21 days, and *C. punctata, Oesophagostomum radiatum,* and *Dictyocaulus viviparus* for 28 days after treatment. *Swine:* For treatment and control of gastrointestinal roundworms, lungworms, kidney worms, sucking lice, and mange mites. See package insert for complete indications and directions for use.

Recommended Dose: *Cattle:* 1 mL (10 mg doramectin) per 110 lb of body weight (200 mcg/kg) administered by subcutaneous (SC) or intramuscular (IM) injection in the neck region. Beef Quality Assurance guidelines recommend SC administration as the preferred route. *Swine:* 1 mL (10 mg doramectin) per 75 lb of body weight (300 mcg/kg) administered by IM injection only.

Residue Warnings: *Cattle:* Do not slaughter for human consumption within 35 days of treatment. Not for use in female dairy cattle 20 months of age or older. A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal. *Swine:* Do not slaughter for human consumption within 24 days of treatment.

Precaution: For SC injection in cattle only. For IM injection in swine and cattle.

Store Below 30°C (86°F)

0 87219 02382 2

Distributed by:
Animal Health
Exton, PA 19341, USA
Div. of Pfizer Inc
NY, NY 10017

Made in USA
9811
05-5199-00-X7

Code 128:

055199003

5 7/8" (W) X 3 3/8" (H)

PMS 116	PMS Reflex blue	Black	Icon Black (60% Black)	Pattern Varnish

05-5199-00-X7 Facsimile Draft #2 11/3/98